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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 01/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/745,920	PARKER, KENNETH C.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *30-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-33* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *10* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendments and remarks, filed 8/4/2003 and 10/22/03, are acknowledged. Amended claims 1, 11, 15, 17-19, and 23 are acknowledged.

Applicant's arguments, filed 8/4/2003 and 10/22/03, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-29 are herein under examination.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-29 are rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

As written, the claims 1-27 encompass computer related methods that appear to lack any physical result performed outside of a computer.

As stated in MPEP § 2106, (IV)(2)(b), to be statutory, a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical application in the technological arts is either disclosed in the specification or would

have been known to a skilled artisan (discussed in MPEP § 2106 (IV)(2)(b)(i)), or (B) be limited to a practical application within the technological arts (discussed in MPEP § 2106 (IV)(2)(b)(ii)).

As stated in MPEP § 2106 (IV)(2)(b)(i), the independent physical acts may be post- or pre-computer processing activity as described below:

> A process is statutory if it requires physical acts to be performed outside the computer independent of and following the steps to be performed by a programmed computer, where those acts involve the manipulation of tangible physical objects and result in the object having a different physical attribute or structure. Diamond v. Diehr, 450 U.S. at 187, 209 USPQ at 8. Thus, if a process claim includes one or more post-computer process steps that result in a physical transformation outside the computer (beyond merely conveying the direct result of the computer operation), the claim is clearly statutory.

> Another statutory process is one that requires the measurements of physical objects or activities to be transformed outside of the computer into computer data (In re Gelnovatch, 595 F.2d 32, 41 n.7, 201 USPQ 136, 145 n.7 (CCPA 1979) (data-gathering step did not measure physical phenomenon); Arrhythmia, 958 F.2d at 1056, 22 USPQ2d at 1036), where the data comprises signals corresponding to physical objects or activities external to the computer system, and where the process causes a physical transformation of the signals which are intangible representations of the physical objects or activities. Schrader, 22 F.3d at 294, 30 USPQ2d at 1459 citing with approval Arrhythmia, 958 F.2d at 1058-59, 22 USPQ2d at 1037-38; Abele, 684 F.2d at 909, 214 USPQ at 688; In re Taner, 681 F.2d 787, 790, 214 USPQ 678, 681 (CCPA 1982).

As stated in MPEP § 2106 (IV)(2)(b)(ii), the computer-related process may be limited to a practical application in the technological arts as described below:

> There is always some form of physical transformation within a computer because a computer acts on signals and transforms them during its operation and changes the state of its components during the execution of a process. Even though such a physical transformation occurs within a computer, such activity is not determinative of whether the process is statutory because such transformation alone does not distinguish a statutory computer process from a nonstatutory computer process. What is determinative is not how the computer performs the process, but what the computer does to achieve a practical application. See Arrhythmia, 958 F.2d at 1057, 22 USPQ2d at 1036.

Claims 1-27 do not fulfill either of these statutory requirements and are therefore rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

Claims 1-27 are rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter. As written, the claims appear to be directed to a method that determines a likelihood, or probability, that merely manipulates numbers, abstract concepts or ideas, or signals representing any of the foregoing.

As stated in MPEP § 2106, (IV)(B)(1), if the "acts" of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. Schrader, 22 F.3d at 294-95, 30 USPQ2d at 1458-59. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process.

In practical terms, claims define nonstatutory processes if they:

> – consist solely of mathematical operations without some claimed practical application (i.e., executing a "mathematical algorithm"); or
> – simply manipulate abstract ideas, e.g., a bid (Schrader, 22 F.3d at 293-94, 30 USPQ2d at 1458-59) or a bubble hierarchy (Warmerdam, 33 F.3d at 1360, 31 USPQ2d at 1759), without some claimed practical application.

Claims 1-27 do not fulfill any of these statutory requirements and are therefore rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter.

Claims 28 and 29 are rejected under 35 U.S.C. 101 because the claims are directed to non-statutory subject matter. As written, the claims appear to be directed to information that is nonfunctional descriptive material that is placed on a medium.

MPEP § 2106 IV (B)(1) states "when nonfunctional descriptive material is recorded on some computer-readable medium, it is not statutory since no requisite functionality is present to satisfy the practical application requirement. Merely claiming nonfunctional descriptive material stored in a computer-readable medium does not make it statutory.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 17, 18, and 19 (lines 1-2 of each) recite the phrase "wherein the step of determining comprises" lacks clear antecedent basis. It is unclear if the determination step of claim 1 is referring to the "determining a biomolecule fragment score" (claim 1, line 9) or "determining the likelihood of the presence or absence of said biomolecule" (claim 1, preamble and lines 21-22). Clarification of which specific determination step to be referred to as mentioned in claims 17, 18, and 19 is requested. Claim 20 is also rejected due to its dependence from claim 19. This rejection is necessitated by amendment.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The rejection of claims 1, 4, 7, 21-24, and 28-29 is maintained under 35 U.S.C. 102(a) as being anticipated by Yates, III et al. (P/N 6,017,693). This rejection is maintained and reiterated for reasons of record.

Yates, III et al. disclose a method of using tandem mass spectrometry to determine sequences which are likely to be identical to an experimentally derived peptide (col. 2, lines 22-27). Yates, III et al. disclose introducing an unknown peptide into a first mass spectrometer to separate it from the rest of the sample (col. 2, lines 54-64). The peptide and its fragments are then passed through a second mass spectrometer to obtain an intensity and mass-to-charge ratio (m/z) (col. 3, lines 4-7), which includes mass signals as seen in Figure 5 (col. 3, lines 7-9). Yates, III et al. disclose a method in Figure 2 where an unknown (12) is analyzed in a tandem mass spectrometer (14) to obtain fragment spectrum (16) and compared (24) to the mass spectra (22) of proteins from a protein sequence library (20) on a computer. Yates, III et al. disclose performing this comparison and calculating a closeness-of-fit measure or score for each of a plurality of mass spectra (col. 4, lines 9-16). Yates, III et al. disclose determining if a fragment mass is found in a measured fragment spectrum and scores are generated and sorted in a repeated cycle which results in one or more candidate amino acid sequences (col. 3, lines 21-28). Yates,

III et al. disclose high-scoring candidate sequences (col. 3, lines 29-30). Yates, III et al. disclose a mass tolerance of the unknown peptide from which spectra from known sequences are identified if they fall within this tolerance amount (col. 4, lines 59-67 and Figure 4) which is reasonably interpreted as the biomolecule fragment detection parameter. Yates, III et al. disclose an example using a tolerance of +0.05% of the mass of the unknown peptide used (col. 5, lines 25-26) which is reasonably interpreted as a detection efficiency as stated in claims 7 and 24. Yates, III et al. disclose the high probability or likelihood that the unknown peptide has an identical amino acid sequence to one of the subsequences taken from the protein sequence library due to the high closeness-of-fit score with respect to the spectra comparison (col. 4, lines 16-23). Yates, III et al. further disclose the high probability of the unknown protein and the known protein from the library as being identical or similar with subsequences with high closeness-of-fit scores (col. 4, lines 23-29). Yates, III et al. disclose performing further MS-MS analysis if original scoring procedures do not delineate an answer of protein match (col. 8, lines 53-61) as stated in claim 23.

Yates, III et al. disclose the calculation of closeness-of-fit (56) in Figure 3 and then the selection of sequences with the highest scores (58). Yates, III et al. disclose outputting matching data for sequences with the highest correlation function (62).

Yates, III et al. disclose normalizing the spectrum (col. 4, lines 35-38) which is reasonably interpreted as a form of calibration as in instant claim 4.

Yates, III et al. disclose the above-mentioned procedure as being performed automatically on a computer (col. 4, lines 30-34). Yates, III et al. disclose computational

resources and storage facilities (col. 9, lines 24-49 and col. 21, lines 8-10) as stated in claims 28 and 29.

Thus, Yates, III et al. teach all of the limitations of claims 1, 4, 7, 21-24, and 28-29.

Applicant states that Yates, III et al. do not teach or suggest a method for determining the likelihood of the presence of a biomolecule using a "biomolecule fragment detection parameter." Applicant states that the instant specification (page 2, lines 22-26) makes it clear that the "biomolecule fragment detection parameter" takes into account the likelihood of detecting a biomolecule fragment as a mass signal in the mass spectrum of the sample. This is found unpersuasive as the specification does not state the biomolecule fragment detection parameter takes into account this likelihood of detection, but rather the methods of the present invention, in general, take into account the likelihood of detection (page 2, line 22). The instant specification states the following: "The numerical value associated with the likelihood of detecting a biomolecule fragment from a given biomolecule is referred to as a 'biomolecule fragment detection parameter.'" It is noted that value is *associated with* the likelihood, but not necessarily, *is* the likelihood which leads one of skill in the art to form very broad but still very reasonable interpretations of a term such as "biomolecule fragment detection parameter". When Yates, III et al. disclose comparisons of mass and fragment spectra, closeness-of-fit scores and identification of sequences falling within a tolerant amount, including high-scoring candidate sequences, (see discussion above) which is reasonably interpreted as a biomolecule fragment detection parameter. Applicant states that Yates, III et al. reference does not take into account the likelihood of detecting a peptide as a mass signal in the mass spectrum of a sample

containing that peptide or reflect the general relative mass signal intensity relationships. This is found unpersuasive as the term "likelihood" is an extremely broad term and, as such, the instant claims are to be interpreted with a very broad interpretation. Finding reliability of matches, as the applicant states is present in the Yates, III et al., is indeed a degree of likelihood of biomolecule presence in a sample. Comparisons of mass spectra reflect relationships of the masses involved. Applicant disagrees with the interpretation of a mass tolerance as a detection efficiency. This is found unpersuasive as the Applicant has not pointed to a definition in the specification that defines a detection efficiency. Also, the Applicant has failed to point out an art recognized definition of "detection efficiency". Therefore, one of skill in the art would broadly and reasonably interpret using a tolerance of a certain percent of the mass of the unknown peptide in the Yates, III et al. invention to be reasonably and broadly interpreted as a detection efficiency.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The rejection of claims 1-7, 11-17, 21-24, and 28-29 is maintained under 35 U.S.C. 103(a) as being unpatentable over Yates, III et al. (P/N 6,017,693), in view of Gras et al.

(Electrophoresis 1999, Volume 20) and Wright et al. (P/N 5,710,713). This rejection is maintained and reiterated for reasons of record.

Yates, III et al. as noted above in the 102 rejection teach the limitations of claims 1, 2, 4, 7, 21-24, and 28-29. Yates, III et al. describe identifying 200 of the most intense ions from the experimentally-derived fragment spectrum (col. 4, lines 44-45) as mentioned in claim 14. Yates, III et al. describe the calculation of closeness-of-fit (56) in Figure 3 and then the selection of sequences with the highest scores (58). Yates, III et al. describe outputting matching data for sequences with the highest correlation function (62) which suggests that any scores lower than the highest scores are likely absent and therefore are not outputted (also see Figure 6D) as stated in claim 2. Yates, III et al. do not teach correcting a mass intensity for an isotopic variant (claim 3), removing noise (claim 5), removing artificial background intensity (claim 6), weighted biomolecule scores, fragment counts, and signal intensity scores to determine the likelihood of the presence or absence of a biomolecule as well as determining a relative concentration based on the biomolecule score.

Gras et al. describe a program that identifies a protein based on mass spectra despite chemical modifications (abstract, lines 1-5) which could be an isotopic variant as stated in claim 3. Gras et al. also describe this determination of isotopic variants via software that often comes with the spectrometer (page 3538, col. 1, lines 1-5 and col. 1, third paragraph). Gras et al. describe a trend or baseline as the signal produced if no material entered the mass spectrometer and in the absence of noise (page 3537, col. 2, lines 10-14; page 3538, col. 1, lines 18-24; and Figure 1) which is reasonably interpreted as the removal of noise and background intensity as stated in claims 5 and 6. Gras et al. describe the smoothing out of error functions related to the

mass signals (page 3538, lines 21-26). Gras et al. describe using selected parameters to search proteins in a database that match the experimental spectra and assigning a score to the candidate protein (page 3541, col. 1, paragraph 2). Gras et al. describe the parameters' effects on the quality and efficiency of the identification (page 3541, col. 1, paragraph 3) as mentioned in claims 7 and 24. Gras et al. describe parameters that include the maximum distance between experimental and theoretical masses, the minimum number (or score) of matched peptides necessary for a protein to be selected, and the number of peaks returned by the peak detection program (page 3541, col. 1, paragraph 4). Gras et al. describe eliminating the least likely proteins in the list of candidates using parameters such as the minimum number of matched peptides or number of detected peaks, as well as depending on their thresholds (page 3541, col. 2, paragraph 1). Gras et al. describe the parameter of peak intensity in the mass spectrum as well (page 3542, col. 2, lines 40-44). Gras et al. describe a mass level parameter which characterizes the degree of match between the experimental mass and the peptide mass of the search library protein (page 3541, col. 1, paragraph 3) which is reasonably interpreted as a mass error. Gras et al. describe defining score calculations by determining the most important parameters, their relative weights and how to integrate them all into the score calculation (page 3542, col. 2, lines 20-23). Gras et al. describe counting the number of experimental masses matching theoretical peptide masses (page 3542, col. 2, lines 29-33) which are fragment counts. Gras et al. describe the concept of the more identified masses a protein has in the mass spectrum, the higher is the confidence for its identification (page 3542, col. 2, lines 33-35). Gras et al. describe assigning weights to each peptide mass, depending on the presence of a match resulting in a score calculation (page 3542, col. 2, lines 36-41 and page 3543, col. 2, lines 15-19). Gras et al.

describe taking into account the calibration error of the measuring device, eliminating masses that are too far from the regression line, and repeating this process when the previous no masses were eliminated in the previous step (page 3543, col. 1, paragraph 3). Gras et al. describe identifying proteins via scores obtained of the proteins in a ranked list of candidate proteins (page 3543, col. 2, lines 37-41).

Wright et al. describe the concentration in the mass spectrometer, its use in standardization of the process including relative estimates, and relative errors resulting without a calibration correction (col. 17, lines 6-26) as stated in claim 16.

Yates, III et al. state that interpretation of the fragment spectra so as to produce candidate amino acid sequences is time-consuming, often inaccurate, and highly technical (col. 1, lines 52-59). Yates, III et al. note that relying on human interpretation often means that analysis is relatively slow and lacks strict objectivity (col. 1, lines 59-60). They further state that approaches based on peptide mass mapping are limited to peptide masses derived from an intact homogeneous protein generated by specific and known proteolytic cleavage (col. 1, lines 61-64). Yates, III et al. state that it would be useful to provide a system for correlating fragment spectra with known protein sequences in a fast and objective way (col. 1, lines 65-67). Yates, III et al. invented a spectral interpreting method that could be used with any size peptide (col. 20, lines 59-60). However, Yates, III et al. note that certain variations and modifications could be made to their invention. A skilled artisan in the art would have been motivated to make further improvements to the identification method of spectral data, such as that stated by Yates, III et al. (col. 2, lines 5-27) in order to provide more accurate results as stated by Yates, III et al. (col. 1, lines 52-59). Therefore, it would have been obvious to one having ordinary skill in the art at the

time the invention was made to include features such as correcting a mass intensity for an isotopic variant, removing noise and artificial background intensity, creating weighted biomolecule scores, fragment counts, and signal intensity scores to determine the likelihood of the presence or absence of a biomolecule, as stated by Gras et al., as well as determining a relative concentration based on the biomolecule score, as stated by Wright et al., in order to provide precise and fast determination of peptide masses, even if the peaks are of low intensity and overlap (Gras et al., abstract, lines 6-7) and to provide accurate and precise concentration estimates (Wright et al., col. 17, lines 19-21) to create more accurate results in mass spectral identification, as stated by Yates, III et al. (col. 1, lines 52-59).

Thus, Yates, III et al., in view of Gras et al. and Wright et al. motivate the limitations of claims 1-7, 11-17, 21-24, and 28-29.

Applicant states neither prior art reference teaches or suggests using a "biomolecule fragment detection parameter". The Applicant has not argued the 103 rejection beyond the argument regarding the "biomolecule fragment detection parameter" phrase. This is found unpersuasive as reiterated from the 35 USC 102(a) discussion above and is equivalently unpersuasive regarding the 103 rejection.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the

Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (703) 308-6043. The examiner can normally be reached Monday through Friday from 8 A.M. to 4:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (703) 305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

January 5, 2004

ARDIN H. MARSCHEL
PRIMARY EXAMINER